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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,982	11/19/2003	Binie V. Lipps	FWLPAT019US	6836

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EXAMINER	
REDDIG, PETER J	
ART UNIT	PAPER NUMBER
1642	
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09/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/716,982	**Applicant(s)** LIPPS ET AL.	
	Examiner PETER J. REDDIG	**Art Unit** 1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 23 June 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *18 August 2008*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): see section 3 of continuation sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-3,8-12,16,17,20 and 24*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☒ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). 6/23/2008
13. ☐ Other: _____.

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/Karen A Canella/
Primary Examiner, Art Unit 1643

Continuation of 11. does NOT place the application in condition for allowance because: 1. Claims 1-3, 8-12, 16, 17, 20 and 24 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the reasons set forth in the Office Action April 14, 2008, section 6, pages 3-10.

Applicants argue that each of the claims is directed toward "A non-invasive cancer screening method". The difference between a screening method and a diagnostic method is that a screening method assigns nonsymptomatic patients to a risk category, whereas a diagnostic method determines whether or not a patient has a disease. The arguments set forth in section 6 relate largely to diagnostic methods, which is not the nature of the invention. When the claimed screening method is carried out, a patient that has a test result over a predetermined value (for example, 1000) is at higher risk for cancer than a patient that has a test result of less than a predetermined value (for example, less than 1000). As is well known to those skilled in the art, (persons possessing doctorate degrees and several years of experience) the predetermined value can be moved higher to reduce the number of false positivetest results, or lower it to reduce the number of false negative test results. There is no magic number, and the failure of the specification to provide one does not establish a meritorious case of nonenablement. Based on the description and examples, and the skill level of the art, a suitable predetermined value for the screening test cutoffcan be determined without unreasonable experimentation.

Applicants' arguments have been considered, but have not been found persuasive. Although the method is drawn to screening and one of skill in the art could adjust the cutoff point to reduce the number of false positive test results, or lower it to reduce the number of false negative test results, given that the ELISA titers for the proteonic polyclonal antibodies exhibit significant overlap between samples from what appears to be normal indiviuals, Tables 2 and 3, and cancer patients, Table 4, with titers over 1: 1000 in both groups, one of skill in the art would not predictably be able to use the claim methods for cancer screeing for the reasons previously set forth.

Applicants argue that the examples in the specification show the recovery of proteonic cancer markers used in the making of antibodies from in vitro sources. The claims would include proteonic cancer markers from in vivo sources. Proteonic cancer markers from in vivo sources would be expected to produce more efficacious antibodies for carryiing out the invention than those from in vitro sources, since "real life" antigens would produce antibodies which effective against them. The situation is non-analogous to (non-antibody-based) cancer drug efficacy, where in vitro efficacy is not a good predictor of in vivo efficacy. Additionally, the invention has been demonstrated in a living system, and this is shown in the examples. Because the specification shows antibody operability from PCMs derived from in vitro sources, antibody operability for PCMs derived from in vivo sources is fairly established.

Applicants arguments have been considered, but have not been found persuasive. Although antibodies produced proteonic cancer markers from in vivo sources could potentially be used as claimed, the claims are not so limited and, thus, this argument is not found persuasive. Given that the ELISA titers for the proteonic polyclonal antibodies produced from the in vitro cultured cell lines exhibit significant overlap between samples from what appears to be normal indiviuals, Tables 2 and 3, and cancer patients, Table 4, with titers over 1: 1000 in both groups, one of skill in the art would not predictably be able to use the claim methods for cancer screening for the reasons previously set forth.

2. Claims 1-3, 8-12, 16, 17, 20 and 24 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons set forth in the Office Action of April 14, 2008, section 7, pages 10-12.

Applicants argue that the recitation of the "genus" in the claims must be evaluated in view of the prior art and the level of skill in the art in order to determine whether it is adequately disclosed. Claim 1 recites: "providing a mixture ofproteonie cancer markers from different types of cancer cells, said mixture containing proteonic cancer markers identified and markersnot yet identified". Different types of cancer cells were known to the art. It was known that the cells produced proteonic cancer markers, some of which were known and others not. What was not known was putting these proteonic cancer markers in a mixture. The level of skill in the art is mostly likely a doctorate degree and several years of research experience. Making a mixture of known materials is well within the level of skill. Furthermore, the specification provides a description of 4 "species" within the "'genus" and demonstrates operability for them, and these are set forth in claim 16 as "a mixture of proteonic cancer markers obtained from breast, liver, colon, and ovarian cancers, said mixture containing proteonic cancer markers identified and markers not yet identified." The specification furthermore mentions at page 5, lines 9-14 that the "cell line can be selected from the group consisting of a breast cancer cell line, a lung cancer cell line, a'stomach cancer cell line, a liver cancer cell line, a colon cancer cell line, an ovarian cancer cell line, a cervical cancer cell line, a mouth/pharynx cancer cell line, a skin cancer cell line, a pancreatic cancer cell line, a testes cancer cell line, a brain tumor cell line, and a prostate cancer cell line." Because of these factors, and because of the disclosure of representative species over the scope of the claims, it is submitted that all claims are in compliance with the written description requirement.

Applicants arguments have been considered, but have not been found persuasive because the proteonic markers for making the mixture are not known in the art or taught by the specification. Althoug cancer cells were known in the art and one of skill in the art could make a mixture of lysates from those cells which would potentially contain the claimed known and unknown proteonic markers, the claims are not limited to mixtures of cancer cell lysates. Thus, given cancer cells, even specific cancer cell types, contain a myriad of potential known and unkwown proteonic markes, none of which have been identified, one of skill in the art could not readily visualize the claimed genus, for the reasons previously set forth.

Applicants argue that the Lilly case is not on point, as the unsupported (and un-described) "genus" there was a genetically

claimed, inadequately characterized, composition of matter which was asserted to be novel. The present claims are methods, and the materials employed are known and/or obtainable using the teaching of the specification and characterized functionally and by way of example.

Applicants arguments have been considered, but have not been found persuasive because, as set forth above, the proteonic markers for making the mixture are not known in the art or taught by the specification and thus, one of skill in the art could not readily visualize the claimed genus.

3. The rejection of Claims 1-3, 8-12, 16, 17, 20 and 24 under 35 U.S.C. 112, first paragraph in section 8, page 12-13 in the Office Action of April 14, 2008 has been withdrawn in view of Applicants arguments.